SHORT REPORT

Iodine deficiency associated with parenteral nutrition in extreme preterm infants

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Arch Dis Child Fetal Neonatal Ed 2003;**88**:F56–F57

Infants are in negative iodine balance on current standard regimens of total parenteral nutrition, with a mean iodine intake of 3 μg/kg/day (150 ml/kg/day). The recommended enteral intake of iodine for preterm infants is 30 μg/kg/day. Gastrointestinal absorption of iodine is high, suggesting that parenteral intakes should approach enteral recommendations.

Iodine is essential for synthesis of thyroid hormones, and thyroxine is necessary for brain development. Transient hypothyroxinaemia in preterm infants is characterised by postnatal reductions in serum levels of total thyroxine, free thyroxine, and triiodothyronine, with normal levels of thyroid stimulating hormone.[1] Transient hypothyroxinaemia is present in most infants of < 30 weeks gestation and is characteristically associated with reductions in intelligence quotient scores but also increased risks of cerebral palsy.[2] The cause of transient hypothyroxinaemia is not clear, with contributions from withdrawal of maternal-placental thyroxine transfer, hypothalamic-pituitary-thyroid immaturity, developmental constraints on the synthesis and peripheral metabolism of iodothyronines, non-thyroidal illness, and iodine deficiency.[3]

An enteral intake of at least 30–40 μg iodine/kg/day is required to achieve a positive iodine balance in healthy preterm infants.[4] Younger and sicker infants, 27–30 weeks gestation, can be in negative iodine balance for the first weeks, and 30 μg iodine/kg/day is the recommended enteral intake for extreme preterm infants.[3] Increasing enteral intakes further to 40–50 μg iodine/kg/day in more mature preterm infants does not alter serum iodothyronine levels.[5] Infants who were parenterally fed were excluded from all these studies. We now report iodine intakes and urinary iodine outputs in a cohort of infants of ⩽ 30 weeks gestation who were initially parenterally fed.

PATIENTS AND METHODS

Thirteen consecutive inborn infants were recruited: male/female ratio, 6:7; gestation mean, 26.8 weeks (range 24–29); birth weight mean, 926 g (range 570–1260). All had intensive care support and survived at least 28 days.

On day 1 of life all infants had parenteral dextrose/electrolyte/amino acid solution (Vaminolact; Fresenius Kabi, Runcorn, Cheshire, UK) with a phosphate supplement (Addiphos; Fresenius Kabi). On day 2, and thereafter, this solution was supplemented with water soluble vitamins (Solvito N; Fresenius Kabi) and trace elements (Peditrace; Fresenius Kabi). In tandem, a fat emulsion (Intralipid 20%; Fresenius Kabi) with added fat soluble vitamins (Vitlipid; Fresenius Kabi) was infused, initially at 8 ml/kg/day, increasing maximally to 18 ml/kg/day by day 5. Enteral feeds were started as hourly boluses, 0.5–1 ml, increased as determined by the infants' clinical condition, with reciprocal reductions in parenteral solutions infused. No infant progressed beyond hourly bolus feeds.

A 24 hour iodine balance was calculated for each infant at days 1, 6, 13, and 27. The types and volumes of all enteral and parenteral fluids used were recorded, and the iodine contents determined. Urine volumes per 24 hours were collected, and an aliquot used for iodine estimations. No iodine-containing skin disinfectants were used. All iodine determinations were performed using the method described for serum[6] but with minor modifications depending on the type of sample.[3]

The Tayside Medical Research ethics committee approved the study protocol. Informed written parental consent was obtained.

RESULTS

The volumes and energy intakes of parenteral and enteral feeding solutions were within the ranges expected for extreme preterm infants (table 1).

Iodine intakes were calculated from contents of solutions used: dextrose/electrolyte/amino acid solution on day 1, mean 0.9 μg/dl (range 0.4–2.0), n = 11; on days 2–28, mean 1.6 μg/dl (range 0.4–11.2), n = 37; fat emulsion, mean 4.1 μg/dl (range 1–10), n = 28; expressed breast milk, mean 10.1 μg/dl (range 4–28), n = 13; Cow and Gate Nutriprem 1, mean 20.2 μg/dl (range 15–24), n = 5; red blood cell concentrates, mean 7.1 μg/dl (range 4–10), n = 10; fresh frozen plasma, 0.7 μg/dl, n = 1; Hepsal (CP Pharmaceuticals), mean 3.45 μg/dl (range

Table 1 Types and volumes of enteral and parenteral nutrition fluids at balance days in 13 extreme preterm infants

Postnatal age (days)	Parenteral nutrition		Enteral nutrition		Total nutrition	
	ml/kg/day	kcal/kg/day	ml/kg/day	kcal/kg/day	ml/kg/day	kcal/kg/day
1	79 (56–96)	31 (24–38)	–	–	79 (56–96)	31 (24–38)
6	110 (7–173)	63 (3–104)	42 (0–189)	27 (0–122)	152 (95–209)	91 (53–125)
13	98 (0–152)	51 (0–93)	56 (0–204)	37 (0–133)	154 (101–204)	88 (56–133)
27	65 (0–185)	28 (0–104)	101 (0–196)	65 (0–147)	166 (31–196)	93 (39–147)

Values are mean (range).

Table 2 Iodine balances in 13 preterm infants during the first 27 days of life

	Mean iodine intake (μg/kg/day)	Mean iodine intake (μg/day)	Mean iodine urine output (μg/day)	Iodine balance (μg/day, +/–)
Day 1	1.0 (0.6–1.7)	0.92 (0.6–2.0)	3.1 (1.3–7.8)	–2.19 (–0.4 to –2.8)
Day 6	3.6 (0.5–9.4)	3.24 (0.6–8.2)	5.5 (1.8–8.1)	–2.3 (–0.9 to –4.8)
Day 13	10.0 (1.5–33.4)	10.0 (1.2–39.4)	4.9 (1.6–13.6)	+5.5 (+35.4 to –1.1)
Day 27	19.6 (1.5–38.0)	22.5 (1.5–49.6)	17.2 (4.0–36.8)	+3.3 (+14.1 to –2.4)

Ranges are shown in parentheses. The iodine balance data (last column) were derived from the balances of the individual infants. It is NOT simply the difference between the mean intake (column 2) and mean output (column 3).

0.8–10.4), n = 8; Abidec (Warner Lambert), 8 μg/dl, n = 1; benzylpenicillin (Biochemie Gmbh), mean 9.6 μg/dl, n = 5; caffeine (Tayside Pharmaceutical), mean 10.2 μg/dl, n = 6; ceftazidime (Glaxo Wellcome), 10 μg/dl, n = 1; dopamine (Abbott), 10 μg/dl, n = 1; frusemide (Martindale Pharmaceuticals), 7.5 μg/dl, n = 2; gentamicin (Hoechst Marion Roussel), 11.3 μg/dl, n = 4; indomethacin (Merck Sharp and Dohme), 10 μg/dl, n = 1; insulin (Novo Nordisk), 9 μg/dl, n = 1; Sytron (Link Pharmaceuticals), 1 μg/dl, n = 1; midazolam (Roche Products Ltd), 13 μg/dl, n = 1; vancomycin (Faulding), 7 μg/dl, n = 1.

Mean iodine intake (μg/kg/day) increased with postnatal age, as did mean urinary iodine output (table 2), paralleled by increased enteral nutritional intakes as parenteral nutrition volumes decreased (table 1). Parenteral nutrition supplied 100% of energy intake at day 1, 70% at day 6, 58% at day 13, and 28% at day 27. All 13 infants were in negative iodine balance on day 1, and 12 remained in negative balance at day 6. By day 13, six infants were in negative balance, but by day 28 only three infants remained in negative balance (table 2).

DISCUSSION

The parenteral nutrition solutions used were made by the pharmacy from the component parts, according to the manufacturer's recommendations. Although different batches of both dextrose/electrolyte/amino acid solution and fat emulsion were used, most had iodine contents within a limited range of values. The parenteral trace element additive was Peditrace solution, which contains potassium iodide. The manufacturer's recommended dosage for infants and children weighing 15 kg or less, and 2 days old or older, is 1 ml/kg/day of Peditrace parenteral solution, which contains 1.3 μg/ml potassium iodide equivalent to 1 μg iodide/kg/day.

The recommended enteral intake of iodine for preterm infants based on balance studies is 30 μg/kg/day.[3 4] The main route of excretion of excess absorbed iodine is through urinary output. Stools were not collected for iodine content because a previous study had shown that faecal iodine outputs were relatively small, about 6% and 10% of intake for term and preterm infants respectively.[4] Iodine absorption by the gastrointestinal tract is high, suggesting that there should be a near equivalence of iodine dosage, whether this is by the enteral or parenteral route.

Iodine deficiency contributes to about 30% of the hypothyroxinaemia in enterally fed preterm infants of 27–30 weeks gestation.[3] The percentage contribution of iodine deficiency to hypothyroxinaemia may be greater in our more immature infants who have a very low parenteral iodine supply. We are currently testing the following hypothesis. If extreme preterm infants are supplemented from the first day of life with parenteral iodine to recommended intakes (30 μg/kg/day), this will improve iodine balance and more importantly postnatal serum iodothyronine levels.

ACKNOWLEDGEMENTS

We thank María Jesús Presas for her skilled technical help with iodine determinations. This work was supported by grants from the Scottish Executive, CEC EUTHYROID QLG3-2000-00930, Wellcome Trust, Tenovus (Scotland), and Paediatric Metabolic Research Trust.

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Accepted 19 June 2002

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